

CLAIMS

What is claimed is:

1. An isolated nucleic acid having the sequence of SEQ ID NO.: 1 or a sequence
5 complementary to SEQ ID NO.: 1, wherein the sequence of SEQ ID NO.: 1 encodes a *C. elegans* chloride intracellular channel protein.
2. The nucleic acid of Claim 1, wherein the nucleic acid is a DNA, RNA or a
PNA.
10
3. The nucleic acid of Claim 2, wherein the nucleic acid is single stranded or
double stranded.
4. An isolated nucleic acid encoding a mutant EXC-4 protein, wherein the
15 isolated nucleic acid has a sequence identical to the sequence of SEQ ID NO.: 1, except for
the presence of one or more missense mutations, nonsense mutations, point mutations,
substitutions, deletions, insertions, polymorphisms, or rearrangements.
5. A recombinant expression vector comprising the isolated nucleic acid of
20 Claim 1.
6. A recombinant expression vector comprising the isolated nucleic acid of
Claim 4.
- 25 7. A host cell comprising the recombinant vector of Claim 5.
8. A host cell comprising the recombinant vector of Claim 6.
9. A method of generating an EXC-4 protein, comprising the steps of:
30 (a) introducing the nucleic acid of Claim 1 into a host cell;
(b) culturing the host cell under conditions allowing expression of the nucleic acid;
and

- 39 -

(c) recovering the EXC-4 protein.

10. A method of generating a mutant EXC-4 protein, comprising the steps of:

(a) introducing the nucleic acid of Claim 4 into a host cell;

5 (b) culturing the host cell under conditions allowing expression of the nucleic acid;
and

(c) recovering the mutant EXC-4 protein.

11. A composition comprising an anti-EXC-4 antibody or an antigen binding
10 fragment thereof, wherein the antibody or antibody fragment specifically binds to all or a
portion of the amino acid residues encoded by SEQ ID NO.: 1.

12. The composition of Claim 11, wherein the antibody is a monoclonal antibody.

15 13. The composition of Claim 11, wherein the antibody is a polyclonal antibody.

14. The composition of Claim 11, wherein the antibody is a humanized antibody.

20 15. The composition of Claim 11, wherein the antibody is a chimeric antibody.

16. The composition of Claim 11, wherein the antibody is a single chain antibody.

25 17. The composition of Claim 11, where the antigen binding fragment is a Fab,
F(ab1)2 or Fv fragment.

18. The composition of Claim 11, further comprising a detectable label.

30 19. The composition of Claim 18, wherein the detectable label is an enzymatic
label, a fluorescent label, a chemiluminescent label, a bioluminescent label or a radioactive
label.

20. A method of identifying a putative agent that inhibits CLIC activity, the method comprising the steps of:

5 (a) contacting a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell with an agent of interest, wherein the *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell comprises a wild-type *exc-4* allele;

(b) measuring the resulting levels of EXC-4 activity in the developing *C. elegans* embryo or isolated *C. elegans* excretory cell; and

10 (c) comparing the measured levels of EXC-4 activity in the treated *C. elegans* embryos or isolated excretory cells to levels of EXC-4 activity in a suitable control, wherein a reduced level of EXC-4 activity relative to the suitable control indicates that the agent of interest is a putative agent that inhibits CLIC activity.

15 21. The method of Claim 20, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

22. The method of Claim 20, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

20 23. A method of identifying a putative agent that inhibits CLIC expression or function, the method comprising the steps of:

(a) contacting a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell with an agent of interest, wherein the *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell comprises a wild-type *exc-4* allele; and

25 (b) observing the resulting excretory cell phenotype of the developing *C. elegans* embryo or isolated *C. elegans* excretory cell, wherein an excretory cell phenotype characteristic of an *exc-4* *C. elegans* mutant indicates that the agent of interest is a putative agent that inhibits CLIC expression or function.

30 24. The method of Claim 23, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

25. The method of Claim 24, wherein the agent of interest is a candidate agent for inhibiting angiogenesis in humans.

5 26. The method of Claim 23, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

27. A method of identifying a putative agent that inhibits CLIC expression, the method comprising the steps of:

10 (a) contacting a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell with an agent of interest, wherein the *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell comprises a wild-type *exc-4* allele; and

(b) measuring levels of expression of the *exc-4* allele following contact with the agent of interest, wherein a reduced level of *exc-4* expression as compared to a suitable control
15 indicates that the agent of interest is a putative agent that inhibits CLIC expression.

28. The method of Claim 27, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

20 29. The method of Claim 28, wherein the agent of interest is a candidate agent for inhibiting angiogenesis in humans.

30. The method of Claim 27, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

25 31. A method of determining whether a CLIC gene is involved in tubulogenesis, comprising the steps of:

(a) providing an embryonic *exc-4* mutant of *C. elegans* or an isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*;

30 (b) expressing a CLIC gene in the embryonic *exc-4* mutant of *C. elegans* or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*, wherein the CLIC gene is operatively linked to a *C. elegans* promoter; and

(c) observing the resulting excretory cell phenotype of the developing embryonic *exc-4* mutant of *C. elegans* or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*, wherein an excretory cell phenotype characteristic of wild-type *exc-4* expression indicates that the CLIC gene is involved in tubulogenesis.

5

32. The method of Claim 31, wherein the CLIC gene is from a human.

33. The method of Claim 32, wherein the human CLIC gene is one of human CLIC 1, human CLIC 2, human CLIC 3, human CLIC 4, human CLIC 5, or human CLIC 6.

10

34. A method of identifying a putative agent that inhibits CLIC expression or function, the method comprising the steps of:

(a) providing a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell, wherein the *C. elegans* embryo is an *exc-4* mutant or the isolated *C. elegans* embryonic excretory cell is derived from an *exc-4* mutant;

15

(b) expressing a CLIC gene in the embryonic *exc-4* mutant of *C. elegans* or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*, wherein the CLIC gene is operatively linked to a *C. elegans* promoter and expression of the CLIC gene rescues the *exc-4* mutant phenotype;

20

(c) contacting the embryonic *exc-4* mutant of *C. elegans* expressing the CLIC gene or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans* expressing the CLIC gene with an agent of interest; and

(c) observing the resulting excretory cell phenotype of the developing embryonic *exc-4* mutant of *C. elegans* or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*, wherein a reversionary excretory cell phenotype characteristic of an *exc-4* *C. elegans* mutant indicates that the agent of interest is a putative agent that inhibits CLIC expression or function.

25

35. The method of Claim 34, wherein the CLIC gene is from a human.

30

36. The method of Claim 35, wherein the human CLIC gene is one of human CLIC 1, human CLIC 2, human CLIC 3, human CLIC 4, human CLIC 5, or human CLIC 6.

37. The method of Claim 34, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

5 38. The method of Claim 37, wherein the agent of interest is a candidate agent for inhibiting angiogenesis in humans.

39. The method of Claim 34, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.